UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,731	01/06/2006	Else Marie Agger	PLOUG8.001APC	1203

20995 7590 06/13/2008

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
06/13/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
eOAPilot@kmob.com

Office Action Summary	Application No.	Applicant(s)	
	10/563,731	AGGER ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4 and 6-17* is/are pending in the application.

4a) Of the above claim(s) *12,16 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6-11 and 13-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/3/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

2. New corrected drawings are required in this application because Figures 6 and 9 have graphs with no data disclosed on them. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Objections

3. Claim 4 is objected to because of the following informalities: As to claim 1, the claim contains the acronym DDA, DODA, DC-chol or DOTAP. While acronyms are permissible shorthand in the claims, the first recitation should include the full recitation followed by the acronym in parenthesis. Appropriate correction is required.

Specification

4. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Information Disclosure Statement

5. The information disclosure statement filed 11/3/2006 has been considered. An initialed copy is enclosed.

Election/Restrictions

6. Applicant's election without traverse of Group I claims 1-2, 4, 6-11, and 13-15 is acknowledged.

Claims 12 and 16-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group II (claim 12), and Group III (claims 16-17), there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement on 2/28/2008.

It is noted that in the restriction filed on 11/1/2007, that there was no species election requested by Examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claims 8 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabled for any vaccine comprising an antigenic component comprising an antigenic epitope from a virulent mycobacterium or for an improved vaccine for cancer, allergy, or an autoimmune disease, wherein the improvement comprises the adjuvant.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

(A) The breadth of the claims;
(B)The nature of the invention;
(C)The state of the prior art;
(D)The level of one of ordinary skill;
(E)The level of predictability in the art;
(F)The amount of direction provided by the inventor;
(G)The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Breadth of the claims: The claims are broadly drawn to a vaccine comprising an any antigenic component comprising an any antigenic epitope from a virulent mycobacterium species or for an improved vaccine for any type of cancer, allergy, or an any type of autoimmune disease, wherein the improvement comprises the adjuvant.

The nature of the invention: The claims are drawn to a vaccine comprising an antigenic component comprising an antigenic epitope from a virulent mycobacterium or for an improved vaccine for cancer, allergy, or an autoimmune disease, wherein the improvement comprises the adjuvant.

The state of the prior art: The art discloses defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that can elicit a particular immune response (i.e. generation of an

antibody that binds to a given epitope) can only be identified empirically (Greenspan et al. 1999 Nature Biotechnology 17: 936-937). The art as at the time of filing teaches that : Although many investigators have tried to develop vaccines based on specific antigens, it is well understood that the ability of an antigen to stimulate antibody production does not necessarily correlate with the ability of the antigen to stimulate an immune response capable of protecting an animal from infection (Chandrashekar et al., US Patent 6,248,329, col. 1, lines 35-41). It is well recognized in the vaccine art, that it is unclear whether an antigen derived from a pathogen will elicit protective immunity. Ellis (Chapter 29 of Vaccines, Plotkin, et al. (eds) WB Saunders, Philadelphia, 1998, especially p. 571, paragraph 2) exemplifies this problem in the recitation that "the key to the problem (of vaccine development) is the identification of that protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies.., and thus protect the host against attack by the pathogen. Furthermore, A vaccine "must by definition trigger an immunoprotective response in the host vaccinated; mere antigenic response is not enough." In re Wright, 999 F.2d 1557,1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology. Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome and form immunoepitopes. Bowie et al. further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no

substitutions (column 2, page 1306). Sprott et al teach a vcaccine adjuvant properties of lipsomes formed at elevated temperatures from the polar chloroform extractable lipids from mycobacterium bovis bacillus calmette-guerin to treat mycobacteria infections (see US Patent Application 20040191304 A1). However the prior art does not teach adjuvant to treat a vaccine comprising an any antigenic component comprising an any antigenic epitope from a virulent mycobacterium species or for an improved vaccine for any type of cancer, allergy, or an any type of autoimmune disease, wherein the improvement comprises the adjuvant. Therefore the state of the art questions if a vaccine comprising an antigenic component comprising an antigenic epitope from a virulent mycobacterium or for an improved vaccine can treat for cancer, allergy, or an autoimmune disease. For the reasons set forth supra, the state of the art is has limitations to a vaccine comprising the claimed invention as set forth supra.

Guidance in the specification The specification discloses immunization with the hybrid Ag85b-ESAT6. The specification disclose the use of lipid from M. Bovis BCG for immunization of Mice. However the specification does not give any examples of administering the vaccine comprising an antigenic component comprising an antigenic epitope from a virulent mycobacterium or for an improved vaccine to treat cancer, allergy, or an autoimmune disease. Therefore, the specification as filed fails to provide particular guidance demonstrating a reasonable extrapolation, which resolves the known unpredictability in the art.

Working examples The specification fails to provide working examples to the subject matter being sought in the claims in the context of a vaccine comprising an antigenic component comprising an antigenic epitope from a virulent mycobacterium or for an improved vaccine for cancer, allergy, or an autoimmune disease, wherein the improvement comprises the adjuvant.

In conclusion, the claimed inventions are not enabled for any vaccine comprising an antigenic component comprising an antigenic epitope from a virulent mycobacterium

or for an improved vaccine for cancer, allergy, or an autoimmune disease, wherein the improvement comprises the adjuvant. The claims are broadly drawn to a vaccine comprising an any antigenic component comprising an any antigenic epitope from a virulent mycobacterium species or for an improved vaccine for any type of cancer, allergy, or an any type of autoimmune disease, wherein the improvement comprises the adjuvant. The specification does not give any examples of administering invention as claimed nor state what amount is considered to be therapeutically effective in a human, the route of administration and time course of administration, the sites of administration, and successful uptake of the immunogenic composition formulated as a vaccine. As a result, for the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods.

Claim Rejections - 35 USC § 102 and 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 4, 6-7, 10-11, and 13 rejected under 35 U.S.C. 102(b) as being anticipated by Liu et al US Patent Application 20020044951 Date April 18, 2002.

Claims 1, 4, 6-7, 10-11, and 13 are drawn to an adjuvant comprising a cationic surfactant and an apolar fraction or part of the apolar fraction of a total lipid extract of a mycobacterium.

Liu et al teach an adjuvant comprising a cationic surfactant (DOTAP) (see [0049] and an apolar fraction or part of total lipid extract of a mycobacterium (see abstract, [0031], [0059]). Lui et al teach a vaccine comprising the adjuvant, wherein vaccine is formulated for parenteral, oral or mucosal administration (see 0048, 0054). Liu et al teach an improved vaccine for an autoimmune disease, wherein the improvement comprises the adjuvant (see 0020-0028). Liu et al teach a delivery system comprising the an adjuvant (see 0045). Liu et al teach an adjuvant wherein mycobacterium is *M. tuberculosis* (see claims).

9. Claims 1, 4, 6-11, 13 and 15 rejected under 35 U.S.C. 103(a) as being unpatentable by Liu et al US Patent Application 20020044951 Date April 18, 2002 in view of Anderson et al US Patent Application 20020176867 Date November 28, 2002.

Claims 1, 4, 6-7, 10-11, and 13 are drawn to an adjuvant comprising a cationic surfactant and an apolar fraction or part of the apolar fraction of a total lipid extract of a mycobacterium.

Liu et al is relied upon as set forth supra. However Liu et al does not teach an adjuvant, wherein the vaccine comprises an antigenic component comprising an antigenic epitope from a virulent mycobacterium, wherein the antigenic component comprises an ESAT6-Ag85B hybrid or a fragment thereof, wherein said virulent bacterium is selected from the group consisting of M. tuberculosis, M. bovis and M. africanum.

Anderson et al teach a tuberculosis vaccine of immunodominant antigens ESAT-6 and Ag85B from Mycobacterium tuberculosis. Anderson et al teach a vaccine, wherein the antigenic component comprising an antigenic epitope from a virulent mycobacterium, wherein the antigenic component comprises an ESAT6-Ag85B hybrid, wherein said virulent bacterium is selected from the group consisting of M. tuberculosis (see title, abstract, claims, 0027, 0079, whole document in its entirety).

It would have been prima facie obvious at the time the invention was made to incorporate a virulent component as taught by Anderson et al into the adjuvant as taught by Liu et al because Liu et al and Anderson et al both teach vaccine composition to treat autoimmune diseases.

10. Claims 1, 2, and 14 rejected under 35 U.S.C. 103(a) as being unpatentable by Liu et al US Patent Application 20020044951 Date April 18, 2002 in view of Ravindranath et al US Patent No. 6218166.

Claims 1, 2, and 14 are drawn to an adjuvant comprising a cationic surfactant and an apolar fraction or part of the apolar fraction of a total lipid extract of a mycobacterium.

Liu et al is relied upon as set forth supra. However Liu et al does not teach an adjuvant, wherein the part of the apolar fraction of the lipid extract is selected from the group consisting of phthiocerol dimycocerosates, trehalose mycolipenates, glycosylated phenol phthiocerols, thehalose mycolates, sulfolipids, triacylglycerols and menaquinones, wherein said glycosylated phenol phthiocerols are phenolic glycolipids, wherein said virulent bacterium is selected from the group consisting of M. tuberculosis, M. bovis and M. africanum.

Ravindranath et al teach adjuvant-incorporated cell composition and methods for enhancing the antibody and T cell response to cellular antigens by incorporating an immunopotentiating agent into the cellular membrane or into an intracellular compartment to increase immune responses against.

Ravindranath et al teach an adjuvant, wherein part or whole of cell of Mycobacterial species of phenolic glycolipids wherein the part of the apolar fraction of the lipid extract is glycosylated phenol phthiocerols, wherein said glycosylated phenol phthiocerols are phenolic glycolipids.

It would have been prima facie obvious at the time the invention was made to incorporate a phenolic glycolipids as taught by Ravindranath et al into the adjuvant as taught by Liu et al because Ravindranath et al teach adjuvant comprising phenolic glycolipids are useful can be conjugated to cellular vaccines.

Status of the Claims

11. No claims are allowed.

Claims 1-2, 4, 6-11, 13-15 are rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina Archie
Examiner
Art Unit 1645

/Nina A Archie/
Examiner, Art Unit 1645
/N. A. A./
Examiner, Art Unit 1645

/Mark Navarro/
Primary Examiner, Art Unit 1645